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AGE, RACE AND SEASON PREDICT VITAMIN D STATUS IN AFRICAN AMERICAN AND WHITE OCTOGENARIANS AND CENTENARIANS

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FOR THE GEORGIA CENTENARIAN STUDY

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Abstract: *Objective:* Poor vitamin D status has been associated with osteoporosis, falls, cardiovascular diseases, cancer, autoimmune diseases, pain, nursing home placement, and other age-related conditions, but little is known about the prevalence and predictors of vitamin D status in those aged 80 and older. Thus, this study tested the hypothesis that vitamin D status would be 1) poorer in a population-based multi-ethnic sample of centenarians as compared with octogenarians and 2) predicted by specific dietary, demographic or environmental factors. *Design:* Cross-sectional population-based analyses. *Setting:* Northern Georgia in the United States. *Participants:* Men and women aged 80 to 89 (octogenarians, n = 80) and 98 and older (centenarians, n = 237). *Measurements:* Regression analyses were used to examine the associations of serum 25-hydroxyvitamin D [25(OH)D] with age, gender, race, living arrangements, dairy food intake, supplement intake, and season. *Results:* The prevalence of vitamin D insufficiency [25(OH)D < 50 nmol/L] was higher in centenarians than in octogenarians ($p < 0.02$). In logistic regression analyses, the risk of being vitamin D insufficient was significantly increased by being a centenarian vs. octogenarian ($p<0.005$) and by being African American vs. white ($p < 0.001$) and decreased by taking a supplement with vitamin D ($p < 0.001$) or by having vitamin D status measured in the summer or fall (each $p < 0.05$), compared with spring. *Conclusions:* Centenarians and octogenarians are at high risk for vitamin D insufficiency for many of the same reasons identified in younger populations. Given the numerous potential adverse consequences of poor vitamin D status, efforts are needed to ensure vitamin D adequacy in these older adults.

Key words: Centenarians, elderly, 25(OH)vitamin D, nutrition risk factors, nutrition supplements.

Introduction

Despite the growing number of centenarians (1), little is known about their nutritional status. Several investigators have explored nutrition-related factors such as low energy intakes (2), antioxidant status (3-5), and cardiovascular diseases in centenarians and their offspring (6-9). However, common nutritional problems in older adults, such as poor vitamin D status, have received little attention in centenarians. A study from Italy suggested that the vast majority of centenarians may have vitamin D deficiency (10, 11), but to our knowledge there are no reported studies of vitamin D status in centenarians in the United States.

Poor vitamin D status is prevalent in older adults and has been associated with osteoporosis, falls, cardiovascular diseases, cancer, autoimmune diseases, pain, depression, weakness, and other age-related conditions (12-18). Risk factors for poor vitamin D status include low vitamin D synthesis in the skin, dark skin color, and low intake from foods and supplements. Older people are at high risk for vitamin D deficiency because they have a reduced capacity to produce vitamin D precursors in the skin from UV light and have low intakes of vitamin D (12). Darker pigmented individuals and people who use sunscreen properly also are at high risk for vitamin D deficiency (12, 13). Vitamin D deficiency can occur among people who live in sunny climates at low latitudes (14, 15) and is quite prevalent among those receiving home-delivered meals (14) and residents of nursing homes and skilled nursing facilities (19-22).

The objective of this study was to determine the prevalence and predictors of poor vitamin D status in a population based multi-ethnic sample of adults aged 80 to 89 and 98 and above from northern Georgia in the US. It was hypothesized that vitamin D deficiency would be prevalent and that age, gender, race, living arrangements (community or skilled nursing facility), dairy food intake, supplement use, and season would predict vitamin D status. Vitamin D status was accessed by measuring serum 25-hydroxyvitamin D [25(OH)D] concentration, which is the preferred biomarker of vitamin D status and assesses vitamin D input from cutaneous synthesis and dietary and supplemental sources (12,13,16). The suggested optimal concentration may be as high as 80 nmol/L, insufficiency is considered less than 50 nmol/L, and frank deficiency is less than 25 nmol/L (12, 13, 16, 18, 23).

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Methods

Study Population

Study participants were part of the Georgia Centenarian Study, a population-based multidisciplinary study of centenarians conducted in 44 counties in northern Georgia (USA) from 2002 to 2005. The study included 244 centenarians (defined in this study as age 98 and older) and 80 octogenarians recruited from the community, personal care homes and skilled nursing facilities. The sampling procedures and data collection methods have been described elsewhere (24). All questionnaires and procedures were approved by the University of Georgia Institutional Review Board on Human Subjects.

Serum Vitamin D

Non-fasting blood samples were collected from the centenarians and octogenarians in their place of residence, allowed to clot at room temperature for 30 min, and transported to the laboratory in a chilled biotransport container within 4 hrs of collection (mean transport time was 2.81 and 2.44 hr for octogenarian and centenarians, respectively). Upon arrival in the lab, samples were centrifuged at 800 x g for 20 min to separate the serum and clot, and the serum was stored at -80º C until time of assay. Serum concentrations of 25(OH)D concentrations were measured by radioimmunoassay (RIA kit, Diasorin Laboratories, Stillwater, MN, USA), similar to the method used for NHANES III (25). This method detects both the D2 and D3 forms of vitamin D metabolites and thus detects vitamin D derived from the diet, dietary supplements and fortified foods as well as that formed in vivo by UV exposure (26). The inter-assay and intra-assay coefficients of variation for 25(OH)D in the present study were 9.2% to 9.5% and 3.8% to 8.0%, respectively.

Various ranges for frank deficiency, insufficiency, and optimal serum concentrations of 25(OH)D have been suggested by others (12,13,16,18,23,27). Based on these suggestions, we defined frank deficiency as < 25 nmol/L, insufficiency as < 50 nmol/L, and optimal as ≥ 80 nmol/L.

Covariates and Predictors

Covariates and predictors included age (80-89 or ≥ 98 years), gender, and race (white or African American, by design). The proportion of participants from each age group recruited from skilled nursing facilities was based on estimates of the "institutionalized" population of the study area according to the 2000 U.S. Census figures (24). Thus, 15% of the octogenarians and 43% of the centenarians resided in skilled nursing facilities. The remaining "community dwelling" participants resided in private residences and personal care homes.

Questions regarding eating patterns and current medications (including supplement use) were read to each participant (or to his or her caregiver), and the answers were recorded by the interviewer. The question regarding dairy food intake was adapted from the Mini-Nutritional Assessment (28) and was "How many servings of milk, yogurt, or cheese does this individual usually consume?" Response categories were frequency per day or per week. Participants were classified as taking a supplement if they reported using a vitamin D-containing supplement such as a multivitamin and/or a calcium supplement that contained vitamin D. The frequency of use of supplements and the amount of vitamin D in supplements were not determined.

Participants were assessed in 2003, 2004 and 2005. Based on the date of blood collection, samples were coded for season with winter defined as December, January, and February; spring defined as March, April, and May; summer defined as June, July and August; and fall defined as September, October, and November consistent with seasonal classifications from the National Health and Nutrition Examination Survey (29; Kelly Scanlon, personal communication).

Exclusions

In the original sample of 244 centenarians, we excluded seven participants (2.9%) from whom we were unable to obtain sufficient serum for vitamin D assessment, resulting in an analysis sample of 237 centenarians. In the multivariate regression modeling, three centenarians were excluded because of missing data (one was missing supplement information, one was missing dairy food intake, and one was missing both supplement and dairy food intake information). There were no exclusions for the octogenarians and their sample size was 80. The total sample for bivariate analyses was 317 and the total sample for multivariate regression modeling was 314.

Statistical Analyses

Because of the unique nature of the centenarian sample, bivariate analyses of the relationships of the covariates within the octogenarian and centenarian samples were conducted separately. In bivariate analyses, the relationship of mean serum 25(OH)D with age group, gender, race, living arrangements, dairy food intake, and supplement use were compared by Student's T-test and season was compared by ANOVA (Table 1). Significant associations for categorical analyses were determined by Fisher's exact tests (Table 1). Probabilities reported are unadjusted for multiple tests.

Multiple linear regression analysis was used to examine the associations of serum 25(OH)D as a continuous variable with age (0 = octogenarian, 1 = centenarian), gender (0 = male, 1 = female), race (0 = white, 1 = African American), living arrangements (0 = community, 1 = skilled nursing facility), dairy food intake (0 = less than one serving daily, 1 = greater than or equal to one serving daily), takes a vitamin D-containing supplement (0 = no, 1 = yes), and season (Table 2). Logistic regression analyses with serum 25(OH)D as a dichotomous variable (1 = less than 50 nmol/L, and 0 = greater than or equal to 50 nmol/L) was used to examine the associations of vitamin D insufficiency with age (0 = octogenarian, 1 = centenarian), gender, race, living arrangements, dairy food intake, supplement use, and season (Table 3). Season was entered into these models as three dummy variables with spring as the reference category, because it was anticipated that serum vitamin D would be lowest in the spring. The results of these two regression models were similar when dairy food intake was coded as < 2 vs. ≥ 2 or as < 1 vs. ≥ 1 servings daily (data not shown).

Table 1
Selected Participant Characteristics and Vitamin D Status as Assessed by 25(OH)D: The Georgia Centenarian Study[1]

25(OH)D (nmol/L)	80s n	80s All 80s Mean ± SD	80s 25(OH)D < 50 nmol/L %	100s n	100s All 100s Mean ± SD	100s 25(OH)D < 50 nmol/L %
Variable						
Overall[2]	80	75.1 ± 34.3	22.5	237	66.7 ± 34.1	36.7
Gender						
Male	27	74.2 ± 33.2	18.5	37	60.5 ± 27.3	48.6
Female	53	75.5 ± 35.1	24.5	200	67.9 ± 35.1	34.5
p <		NS	NS		NS	0.05
Race						
White	66	78.4 ± 35.4	19.7	190	70.4 ± 33.9	30.5
African American	14	59.6 ± 23.5	35.7	47	52.0 ± 31.1	61.7
p <		0.07	NS		0.001	0.001
Living arrangements						
Community	68	75.6 ± 35.6	22.1	138	64.3 ± 34.6	40.6
Facility	12	72.1 ± 26.7	25.0	99	70.1 ± 33.3	31.3
p <		NS	NS		NS	NS
Dairy intake[3]						
<1/day[3]	20	64.2 ± 33.9	40.0	72	67.9 ± 37.1	36.1
>1/day	60	78.7 ± 33.9	16.7	163	66.3 ± 32.7	36.8
p <		NS	0.05		NS	NS
< 2/day	54	70.6 ± 33.1	24.1	126	64.7 ± 34.7	39.7
> 2/day	26	84.4 ± 35.4	19.2	109	69.1 ± 33.2	33.0
p <		NS	NS		NS	NS
Supplement[4]						
No	42	70.4 ± 36.6	26.2	137	56.2 ± 30.7	48.9
Yes	38	80.2 ± 31.2	18.4	98	81.0 ± 33.6	20.4
p <		NS	NS		0.001	0.001
Seasons[5]						
Winter	14	77.1 ± 14.8	0.0	62	63.1 ± 29.2	37.1
Spring	27	60.6 ± 26.0	37.0	78	59.1 ± 25.5	43.6
Summer	23	82.4 ± 35.8	21.7	61	70.9 ± 37.7	31.1
Fall	16	87.1 ± 48.3	18.8	36	82.6 ± 45.1	30.6
p <		0.05	0.05		0.01	NS

1. Values are unadjusted means and distributions. P values are from Student t-tests for means and from Fischer exact tests for categorical data. NS is not significant; 2. Compared to octogenarians, centenarians tended to have lower serum 25(OH)D (p < 0.07) and a higher prevalence of insufficient serum 25(OH)D (p < 0.02); 3. Dairy is defined as servings of milk, yogurt, and/or cheese daily; 4. Vitamin D supplements, multivitamins, and calcium supplements that also contain vitamin D but excludes calcium only supplements; 5. Seasons: 12/1 through 2/29; Spring: 3/1 through 5/31; Summer: 6/1 through 8/31; Fall: 9/1 through 11/30.

Analyses were conducted with the SAS statistical software (version 8.2, SAS Institute, Cary, NC) and Stata (version 9.2, Stata Corp., College Station, TX).

Results

Compared to the total sample, the centenarian participants who were excluded from the analyses because of missing serum 25(OH)D (n = 7) were more likely to be African American (5 of 7, p < 0.01), reside in a skilled nursing facility (6 of 7, p < 0.01), and take a vitamin D-containing supplement (7 of 7, p < 0.01), but did not differ in their gender or dairy food intake.

Compared to the octogenarians, the centenarians were an average of 17 years older (age range of 98-109 vs. 81-90 and mean age of 101 ± 2 vs. 84 ± 3 for centenarians and octogenarians, respectively; p < 0.001), and were more likely to be women (84.4 vs. 66.2%; p < 0.001), live in a skilled nursing facility (41.8 vs. 15%; p < 0.001), and consume two or more servings of dairy foods daily (46.4 vs. 32.5%; p < 0.02), but their distribution by race (19.8 vs. 17.5% African American) and season of vitamin D assessment (26.2 vs. 17.5% winter, 32.9 vs. 33.8% spring, 25.7 vs. 28.8% summer and 15.2 vs. 20% fall) was not significantly different. Compared to octogenarians, centenarians tended to have lower average serum 25(OH)D concentrations (66.7 vs. 75.1 nmol/L; p < 0.07) and had a higher prevalence of vitamin D insufficiency (serum 25(OH)D < 50 nmol/L, 36.7 vs. 22.5%; p < 0.02). The prevalence of frank vitamin D deficiency (serum 25(OH)D < 25 nmol/L, 8.9 vs. 5% of centenarians and octogenarians, respectively) and of participants with optimal serum concentrations (serum 25(OH)D > 80 nmol/L, 31.2 vs. 37.5% of centenarians and octogenarians, respectively) was not different between the two age groups.

Mean serum 25(OH)D and the prevalence of serum 25(OH)D < 50 nmol/L within octogenarians and within centenarians are shown in unadjusted bivariate analyses in Table 1. Although power was limited to detect associations of the variables of interest within the octogenarian sample, season emerged as a strong predictor of vitamin D status such that serum 25(OH)D was highest in the fall and lowest in the spring (p < 0.05). Race and supplement use emerged as consistent predictors of vitamin D status in centenarians, such that higher vitamin D status was associated with being white vs. African American (p < 0.001) and with taking a supplement vs. not taking a supplement (p < 0.001). In centenarians, season was associated with mean serum 25(OH)D (p < 0.01) and was highest in the fall and lowest in the spring; however, the prevalence of vitamin D insufficiency was not influenced by season.

Many of our predictor variables are themselves associated and bivariate analyses may thus mask important associations. Therefore, we estimated a multiple linear regression model predicting serum 25(OH)D concentrations (Table 2). Vitamin D status was lower in centenarians than octogenarians, and lower among African Americans than whites. Vitamin D status was also higher among those taking a dietary supplement containing vitamin D. Finally, vitamin D status was higher in the summer and fall, relative to the spring.

The prevalence of vitamin D insufficiency was estimated in a logistic regression model (Table 3). In this model, the risk of being vitamin D insufficient was increased by about 2- to 3-fold by being a centenarian vs. octogenarian (OR 2.49, 95% CI 1.29, 4.82, p < 0.005), being African American vs. white (OR 3.50, 95% CI 1.86, 6.57, p < 0.001), and decreased by taking a supplement with vitamin D (OR 0.35, 95% CI 0.19, 0.63, p <

0.001), and having vitamin D status assessed in the summer (OR 0.45, CI 0.23, 0.89, p < 0.02) or fall (OR 0.42, CI 0.19, 0.91, p < 0.03). However, the likelihood of being vitamin D insufficient was not associated with gender, living arrangements, or dairy food intake.

Table 2
Linear Regression Model Predicting Vitamin D Status as Assessed by Serum 25(OH)D: The Georgia Centenarian Study. Adjusted $R^2 = 0.195$

Variable	b	95% CI		t	p
Centenarian	-0.509	-1.006	-0.13	-2.02	0.044
Female	4.713	-4.102	13.528	1.05	0.294
African American	-16.645	-25.501	-7.789	-3.70	0.001
Skilled Nursing Facility	3.204	-4.743	11.151	0.79	0.428
Dairy (≥ 1 serving daily)	-0.074	-7.910	7.761	-0.02	0.985
Supplement with vitamin D	20.539	13.110	27.969	5.44	0.001
Winter	6.245	-2.971	15.461	1.33	0.183
Summer	16.667	7.686	25.649	3.65	0.001
Fall	26.804	16.391	37.219	5.07	0.001
Intercept	98.538	51.339	145.738	4.11	0.001
F(9,304)	9.43				

Table 3
Logistic Regression Model Predicting Vitamin D Insufficiency (Serum 25(OH)D < 50 nmol/L): The Georgia Centenarian Study

Variable	b	LR χ^2	p(χ^2)	Odds Ratio	95% CI	
Centenarian	0.913	7.890	0.005	2.492	1.288	4.821
Female	-0.379	1.290	0.256	0.684	0.357	1.313
African American	1.252	15.560	0.001	3.498	1.863	6.569
Skilled Nursing Facility	-0.296	0.960	0.327	0.744	0.411	1.347
Dairy (≥ 1 serving daily)	-0.113	0.150	0.702	0.893	0.502	1.590
Supplement with vitamin D	-1.062	13.380	0.001	0.346	0.191	0.625
Winter	-0.628	3.350	0.067	0.534	0.270	1.053
Summer	-0.798	5.430	0.020	0.450	0.227	0.891
Fall	-0.876	5.030	0.025	0.417	0.190	0.912
Intercept	-2.191					
LR $\chi^2(9)$	49.06					

Discussion

To our knowledge, this is the first reported study of the vitamin D status of centenarians in the US. The prevalence of vitamin D insufficiency in centenarians was higher than in octogenarians, but the overall vitamin D status of these US centenarians was better than observed for Italian centenarians (10,11). Other major findings include the similar prevalence of vitamin D insufficiency in men and women, the large impact of race and supplement use, the lack of benefit of the reported dairy food intake, and the similar vitamin D status in those residing in the community and in skilled nursing facilities.

Vitamin D insufficiency is of concern in older adults because poor vitamin D status has been associated with many chronic conditions including osteoporosis, falls, cardiovascular diseases, cancer, autoimmune diseases, pain, and nursing home placement (12,13,15,16,18,30). As emphasized by Andersen-Ranberg et al. (31), "It will be a worldwide challenge to make plans for future health and nursing care and it is therefore highly important to provide new insights about the conditions in which future generations will reach the end of human life." Regarding vitamin D specifically as a part of health care, randomized controlled trials provide a high level of evidence for the efficacy of vitamin D supplements for preventing and/or managing significant health problems in the elderly, such as fractures and falls in older adults (32,33). Serum 25(OH)D concentrations less than 75 nmol/L have been associated with a 2- to 3-fold higher risk of nursing home placement in older adults (30). Thus, improvements in vitamin D nutriture could improve the health and independence of older people, including centenarians.

The high prevalence of vitamin D insufficiency in octogenarians (22.5%, unadjusted) and centenarians (36.7%, unadjusted) in Georgia was not unexpected based on national studies of vitamin D status in the US such as the National Health and Nutrition Examination Survey (NHANES) (25). The NHANES studies provide the only national population-based reports of the vitamin D status in the US and the relationship of serum 25(OH)D with age, gender, race, supplement use, and milk intake have been reported for NHANES III (conducted in 1988 to 1994) (25,29). NHANES III reported that mean 25(OH)D concentrations at lower latitudes during winter and at higher latitudes during summer in those aged 80+ were 68.7 and 69.5 nmol/L in men, respectively, and 59.6 and 61.8 nmol/L in women, respectively. The prevalence of vitamin D insufficiency [25(OH)D < 50 nmol/L] in NHANES III in those aged 80+ was 19% to 26% in men and 34% to 37% in women, depending on season. These ranges are similar to our findings, except that 48.6% (unadjusted) of our centenarian men had vitamin D insufficiency (Table 1). Our findings may not be directly comparable to NHANES because NHANES does not sample the nursing home population, Georgia has a higher proportion of African Americans than a nationally representative sample, NHANES III sampled the Hispanic population, the low latitude of Georgia with more abundant sunlight than in the northern US, and different methods of adjusting for covariates.

In a study of centenarians from Italy, 25(OH)D concentrations were 78 nmol/L in one participant receiving vitamin D injections, averaged 16 nmol/L in four centenarians with detectable concentrations, and was not detectable in the remaining 99 individuals (10,11). The high prevalence of vitamin D deficiency was attributed to several factors including rainy weather, not going outside, and lack of vitamin D-fortified foods in Italy. In another Italian study, the InCHIANTI Study (17), serum 25(OH)D averaged 57.9 nmol/L in men and 43.3 nmol/L in women (N = 976, mean age 74.8 years); thus, profound vitamin D deficiency is probably not characteristic of the older adult population in Italy. Some studies of centenarians have measured 1,25-dihydroxyvitamin D, which generally is not considered a good marker of overall vitamin D status (34), so this study cannot be compared to the present study.

Season had a large impact on serum 25(OH)D even after controlling for other factors. This finding suggests that controlling for season of measurement is important at all ages, even among the very old in their 80s and 100s. It was not expected that season would have such a large impact, because we assumed that people in their 80s and 100s would not spend much time outdoors and that their skin would have lost most of its ability to synthesize vitamin D in response to sunlight. However, a study in Japan found that about 10 min daily of natural sunlight exposure in older women with Alzheimer's disease who were chronically hospitalized improved serum 25(OH)D by about 28 nmol/L after one year (from 24.0 to 52.2 nmol/L, latitude 32.0° N) (35). There is concern about skin cancer and sunlight exposure, so some supplementation rather than sunlight exposure has been recommended as the primary source of vitamin D in older adults (18).

The poor vitamin D status in African Americans compared to whites was expected, even after controlling for other factors. Race probably remained as a major predictor of vitamin D status after controlling for season, because darker skin has less capacity to make vitamin D from sunlight (12,18).

The large benefit of vitamin D-containing supplements was expected and has been documented elsewhere in older adults (14,36-38). Because we did not determine the amount of vitamin D in the supplements and the frequency of supplement intake, we cannot quantify vitamin D intake from supplements. Typical multivitamins contain 10 µg of vitamin D (400 IU), while typical vitamin D-containing supplements available during the study period have 2.5 to 5 µg of vitamin D (100 to 200 IU) (18). Given that most participants taking a vitamin D supplement were taking a multivitamin, the contribution from supplements probably averaged about 10 µg. The 2005 Dietary Guidelines for Americans recommends that older adults probably need about 25 µg vitamin D daily (1,000 IU) to reach the optimal 25(OH)D concentration of 80 nmol/L (23).

The lack of a large benefit of dairy food intake on vitamin D status was expected. Milk accounts for the vast majority of dairy food intake in the US, but only has 2.5 µg vitamin D (100 IU) per cup (18). Thus, consumption of one or two cups of milk daily will only contribute a small amount of the 25 µg vitamin D (1,000 IU) recommended daily (23). Also, our measure of dairy food intake was not specific to milk, but also included yogurt and cheese. However, we have previously shown that milk is the primary contributor to dairy food intake by centenarians in Georgia (39). Moreover, milk, but few other dairy foods, is routinely fortified with vitamin D (18).

Based on other studies of the vitamin D status of older people in nursing homes (19,40), we expected that community dwellers would have better vitamin D status than those residing in nursing homes. However, in this study we found that compared to centenarians residing in the community, centenarians in skilled nursing facilities had a superior dietary patterns with higher dairy food intake (41) and they were more likely to take a vitamin D-containing supplement (32.8% vs. 54.1%, unadjusted, $p < 0.01$). Thus, residence in a nursing home is not necessarily a strong risk factor for vitamin D insufficiency when dairy foods (e.g., vitamin D-fortified as indicated milk) and vitamin D-containing supplements are provided.

Limitations of this study include no direct measures of the time spent in the sun or the actual intake of vitamin D from dietary supplements or from foods. However, season and supplement use were robust predictors of vitamin D status.

In summary, a high prevalence of poor vitamin D status was observed among octogenarians and centenarians (a higher prevalence in centenarians than in octogenarians) in a cross-sectional population study. Season of measure influences serum 25(OH)D so strongly that it is possible that measurements in the fall, the highest season of the year, may mask vitamin D insufficiency at other times of the year. Given concerns about the negative impact of poor vitamin D status on health and well being, especially related to fractures, falls, and nursing home placement (30,32,33), efforts to improve the vitamin D status of the very old are needed. In the very old, more research is needed to determine the most appropriate target concentration of serum 25-hydroxyvitamin D (e.g., > 50 nmol/L or > 75 to 80 nmol/L), as well as protocols for screening, prevention, and treatment of poor vitamin D status.

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